09/579 784

Attorney Docket No. 035718/199392 *PATENT*

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Patent Number : 6,911,575 B1

Issued : June 28, 2005

Name of Patentee : Pioneer Hi-Bred International, Inc.

Title of Invention : Targeted Manipulation of Genes in Plants

Certificate
AUG 10 2005
of Correction

Certificate of Corrections Branch
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

REQUEST FOR CERTIFICATE OF CORRECTION OF PATENT FOR PTO MISTAKE (37 CFR 1.322(a))

1. Attached, in duplicate, is Form PTO/SB/44, with at least one copy being suitable for printing.

2. The exact page and line number where the errors are shown correctly in the application file are:

   Claim 1 was amended and is accurately shown on page 2, specifically line 5 of the claim, in the Supplemental Amendment filed October 22, 2004. In the issued patent, column 33, line 18, the word "oncoding" should read "encoding".

A copy of the Supplemental Amendment dated October 22, 2004 and the Notice of Allowance issued January 12, 2005, in response to the above-referenced amendment are attached for the convenience of the office

3. Please send the Certificate to:

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1) Request for Certificate of Correction of Patent for PTO Mistake / 2 Pages (1 copy)
2) Copy of Supplemental Amendment dated October 22, 2004 / 23 Pages (1 copy)
3) Copy of Notice of Allowance / 4 Pages (1 copy)
4) Certificate of Correction /1 Page (2 copies)

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Appl. No.: 09/579,784 Confirmation No.: 9894
Applicant(s): Baszczynski *et al.*
Filed: 5/26/00
Art Unit: 1638
Examiner: D. Kruse
Title: TARGETED MANIPULATION OF GENES IN PLANTS

Docket No.: 035718/199392
Customer No.: 29122

Mail Stop Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

SUPPLEMENTAL AMENDMENT
37 C.F.R. § 1.121

Sir:

This Amendment is in response to the Notice of Incomplete Response mailed October 8, 2004. The amendments and remarks appearing below are identical to those appearing in the Supplemental Amendment filed on July 26, 2004, except that the claim amendments are made from the claims filed in the June 21, 2004 response.

Applicants respectfully request reexamination and reconsideration of the above-identified application in view of the following amendments and remarks. The Examiner is respectfully requested to enter the following amendments.

Amendments to the Claims are reflected in the listing of claims beginning on page 2 of this paper.

Remarks begin on page 7 of this paper.

Amendments to the Claims:

1. (Currently amended) A method to inactivate a nucleotide sequence of interest introduced into a genome of a plant cell, said method comprising:

transforming said plant cell with a nucleic acid molecule comprising a promoter operably linked to said nucleotide sequence of interest~~, wherein said nucleotide sequence of interest encodes~~ encoding a polypeptide capable of conferring herbicide resistance in the plant cell; and

introducing into said plant cell at least one chimeric oligonucleotide, said chimeric oligonucleotide having at least a first block of RNA residues and a second block of RNA residues, wherein said first and said second block of RNA residues are homologous to said ~~nucleotide~~ nucleic acid molecule; said first and said second block of RNA residues are each about 3 nucleotides to about 20 nucleotides in length and are contiguous with and flank a block of DNA residues, wherein the block of DNA residues comprises at least one mismatch to the nucleic acid molecule and said block of DNA residues is about 5 nucleotides to about 60 nucleotides in length; wherein said first RNA block, said DNA block and said second RNA block are identical to a contiguous sequence of the nucleic acid molecule except for the presence of said mismatch in said DNA block; said chimeric oligonucleotide comprises additional DNA residues that are capable of forming a duplex structure with said first block of RNA residues, said block of DNA residues, and said second block of RNA residues; and, said chimeric oligonucleotide being capable of recognizing and implementing a nucleotide conversion in said nucleic acid molecule, whereby said nucleotide conversion in said nucleic acid molecule inactivates the nucleotide sequence of interest encoding the polypeptide capable of conferring herbicide resistance in the plant cell and thereby modulates the herbicide resistance of said plant cell.

2. (Original) The method of claim 1, wherein said nucleotide conversion is in the promoter.

3. (Currently amended) The method of claim 1, wherein said nucleotide conversion is in ~~a~~ the coding region of said nucleotide sequence of interest.

4. (Canceled)

5. (Canceled)

6. (Previously presented) The method of claim 1, wherein the chimeric oligonucleotide introduces a frameshift in the normal reading frame of the nucleotide sequence of interest.

7. (Previously presented) The method of claim 1, wherein the chimeric oligonucleotide introduces a premature stop codon in the normal reading frame of the nucleotide sequence of interest.

8. (Canceled)

9. (Previously presented) The method of claim 1, wherein said nucleotide sequence of interest encodes 5-enol pyruvylshikimate-3-phosphate synthase.

10. (Previously presented) The method of claim 1, wherein said nucleotide sequence of interest encodes acetohydroxy acid synthetase.

11. (Canceled)

12. (Canceled)

13. (Previously presented) The method of claim 1, wherein said plant cell is from a monocot.

14. (Previously presented) The method of claim 13, wherein said monocot is maize.

15. (Previously presented) The method of claim 1, wherein said plant cell is from a dicot.

16. (Currently amended) A method to inactivate a nucleotide sequence of interest introduced into a genome of a plant, said method comprising:

transforming said plant with a nucleic acid molecule comprising a promoter operably linked to said nucleotide sequence of interest encoding, ~~wherein said nucleotide sequence of interest encodes~~ a polypeptide capable of conferring herbicide resistance in the plant; and,

introducing into said plant at least one chimeric oligonucleotide, said chimeric oligonucleotide having at least a first block of RNA residues and a second block of RNA residues, wherein said first and said second block of RNA residues are homologous to said nucleic acid molecule; said first and said second block of RNA residues are each about 3 nucleotides to about 20 nucleotides in length and are contiguous with and flank a block of DNA residues, wherein the block of DNA residues comprises at least one mismatch to the nucleic acid molecule and said block of DNA residues is about 5 nucleotides to about 60 nucleotides in length; wherein said first RNA block, said DNA block and said second RNA block are identical to a contiguous sequence of the nucleic acid molecule except for the presence of said mismatch in said DNA block; said chimeric oligonucleotide comprises additional DNA residues that are capable of forming a duplex structure with said first block of RNA residues, said block of DNA residues, and said second block of RNA residues; and, said chimeric oligonucleotide being capable of recognizing and implementing a nucleotide conversion in said nucleic acid molecule, whereby said nucleotide conversion in ~~is~~ said nucleic acid molecule inactivates the nucleotide

sequence of interest encoding the polypeptide capable of conferring herbicide resistance in the plant and thereby modulates the herbicide resistance of the plant.

17. (Previously presented) The method of claim 16, wherein said nucleotide conversion is in the promoter.

18. (Currently amended) The method of claim 16, wherein said nucleotide conversion is in a the coding region of said nucleotide sequence of interest.

19. (Previously presented) The method of claim 16, wherein the chimeric oligonucleotide introduces a frameshift in the normal reading frame of the nucleotide sequence of interest.

20. (Previously presented) The method of claim 16, wherein the chimeric oligonucleotide introduces a premature stop codon in the normal reading frame of the nucleotide sequence of interest.

21. (Canceled)

22. (Canceled)

23. (Previously presented) The method of claim 16, wherein said nucleotide sequence of interest encodes 5-enol pyruvylshikimate-3-phosphate synthase.

24. (Previously presented) The method of claim 16, wherein said nucleotide sequence of interest encodes acetohydroxy acid synthetase.

25. (Canceled)

26. (Canceled)

27. (Previously presented) The method of claim 16, wherein said plant is a monocot.

28. (Previously presented) The method of claim 27, wherein said monocot is maize.

29. (Previously presented) The method of claim 16, wherein said plant is a dicot.

REMARKS

Status of the Claims

Claims 1-29 were rejected. Claims 4, 5, 8, 11, 12, 21, 22, 25, and 26 have been canceled without prejudice or disclaimer. Applicants reserve the right to pursue the subject matter of claims 4, 5, 8, 11, 12, 21, 22, 25, and 26 in a continuation or divisional application.

Claims 1 and 16 have been amended. Specifically, claims 1 and 16 have been amended to recite that the chimeric oligonucleotide is capable of recognizing and implementing a nucleotide conversion in the nucleic acid molecule, whereby said nucleotide conversion in said nucleic acid molecule "inactivates the nucleotide sequence of interest encoding the polypeptide capable of conferring herbicide resistance in the plant cell [or plant] and thereby" modulates the herbicide resistance of the plant or plant cell. Support for this amendment can be found, for example, on page 9, lines 25-34 of the specification.

Claims 3 and 18 were amended to recite "the" coding region.

No new matter has been added by way of these amendments.

The Objections to the Specification Should Be Withdrawn

The specification was objected to for the incorporation of essential material in the specification by reference to a foreign application, foreign patent or to a publication. Specifically, the Examiner objects to page 11, lines 29-30 and page 32, lines 17-20. This objection is respectfully traversed.

As outlined in MPEP 608.01(o):

> "essential material" is defined as that which is necessary to (1) describe the claimed invention, (2) provide an enabling disclosure of the claimed invention, or (3) describe the best mode (35 U.S.C. 112)... Nonessential subject matter may be incorporated by reference to (1) patents or applications published by the United States or foreign countries or regional patent offices, (2) prior filed, commonly owned U.S. applications, or (3) non - patent publications. *Nonessential subject matter is subject matter referred to for purposes of indicating the background of the invention or illustrating the state of the art* (emphasis added).

Page 11, lines 29-30 refers to WO 97/04103 which discloses a glyphosate resistance gene carrying double mutations. This WO publication simply reflects the state of the art. In fact, Figure 3 and 4 of the present invention provide non-limiting examples of chimeric oligonucleotides that are designed to alter the amino acids disclosed in WO 97/04103. It is clear the reference being cited by the Examiner represents nonessential material, and the objection should be withdrawn.

The Rejection of the Claims Under 35 U.S.C. §112, Second Paragraph, Should Be Withdrawn

Claims 3-5, 8, 18, 21 and 22 were rejected under 35 U.S.C. §112, second paragraph, for indefiniteness. This rejection is respectfully traversed.

Claim 3 was rejected for the term "a coding region." The Examiner states that the metes and bounds of this term are not clear, but offers no further explanation. To determine the acceptability of claim language, one must determine if one of skill in the art would understand what is claimed in view of the specification. The term "a coding region" is standard term used in the art to describe a region of a nucleotide sequence that can be translated into a polypeptide. As such, the term is clear, and the rejection of claim 3 should be withdrawn. During the telephonic interview of July 13, 2004, the Examiner stated that the objection for the term would be withdrawn if "a coding region" was amended to recite "the coding region." The claims have been amended as suggested by the Examiner, and the objection has been obviated.

Claims 4 and 21 were rejected for the term "comprises." Claims 4 and 21 have been canceled, and the objection has been obviated.

Claims 5 and 22 were rejected for the term "modifies." Claims 5 and 22 have been canceled, and the rejection has been obviated.

Claim 8 was rejected for the term "a region of the promoter critical for transcription." Claim 8 has been canceled, and the rejection has been obviated.

The Rejection of the Claims Under 35 U.S.C. §112, First Paragraph, Should Be Withdrawn

Written Description

Claims 1-10, 13-24, and 27-29 were rejected under 35 U.S.C. §112, first paragraph, for lack of written description. The Examiner asserts that the "chimeric oligonucleotides encompassed by the claimed method are only described by general structure" and therefore do not satisfy the written description standard. This rejection is respectfully traversed.

I. Independent claims 1 and 16 have been amended to recite that the "nucleotide sequence of interest encodes a polypeptide capable of conferring herbicide resistance" in the plant or plant cell and that the chimeric oligonucleotide when introduced into the plant or plant cell is capable of producing a nucleotide conversion in the nucleic acid molecule that "inactivates the nucleotide sequence of interest encoding the polypeptide capable of conferring herbicide resistance in said plant cell [or plant cell] and thereby modulates the herbicide resistance of the plant [or plant cell]." For the reasons outlined below, the chimeric oligonucleotide recited in the amended claimed method has a defined structure based on the nucleotide sequence that is capable of conferring herbicide resistance.

The Examiner states that the chimeric oligonucleotides recited in the claimed methods are described by only a "general structure" and that "biomolecule sequences described only by functional characteristics, without any known or disclosed correlation between that function and structure of the sequences, normally is not sufficient even when accompanied by a method of obtaining the claimed sequence." For the reasons previously made of record Applicants disagree that the common structural and functional characteristics shared among members of the chimeric oligonucleotides recited in the claimed methods is insufficient to satisfy the written description requirements. However to expedite prosecution, independent claims 1 and 16 have been amended to recite that the RNA residues of the chimeric oligonucleotide are homologous to a nucleotide sequence of interest that encodes a polypeptide" capable of conferring herbicide resistance." As amended, the claims provide a clear description of the class of target sequences

that will be targeted in the claimed method and thereby satisfy the written description requirement.

The Federal Circuit has made it clear that sufficient written description requires simply the knowledge and level of skill in the art to permit one of skill to immediately envision the product claimed from the disclosure. *Purdue Pharm L.P. v. Faulding In.*, 230 F.3d 1320 1323, 596 USPQ2d 1481, 1483 (Fed. Cir. 2000) ("One skilled in the art must immediately discern the limitations at issue in the claims."). In fact, in Amgen, 57 USPQ2d (Fed. Cir. 2003), in affirming the district court's holding that claims to a recombinant protein that are prepared in vertebrate or mammalian cells complies with the Written Description requirement the majority stated:

> Both Eli Lilly and Enzo Biochem are inapposite to this case because *the claim terms at issue are not new or unknown biological materials that ordinarily skilled artisans would easily miscomprehend.* Instead, the claims of Amgen's patents refer to types of cells that can be used to produce recombinant human EPO. Thus, TKT can only challenge the adequacy of disclosure of the vertebrate or mammalian host cell—not the human DNA itself. This difference alone sufficiently distinguishes Eli Lilly, because when used, as here, merely to identify types of cells (instead of undescribed, previously unknown DNA sequences), the words "vertebrate" and "mammalian" readily "convey[] distinguishing information concerning [their] identity" such that one of ordinary skill in the art could visualize or recognize the identity of the members of the genus." *Eli Lilly,* 43 USPQ2d at 1406. Amgen, 57 USPQ2d at 1507 (emphasis added).

In the instant case, the claims have been amended to recite that the nucleotide sequence of interest encodes a polypeptide that is capable of conferring herbicide resistance in a plant. This term *does not refer to a new or unknown biological material that ordinary skilled artisans would easily miscomprehend.* The lines of evidence to arrive at this conclusion are briefly summarized below.

1. The specification provides several nucleotide sequences that confer resistance to various herbicides including sulfonylurea, imidazolinone, and glyphosate. The exemplary sequences disclosed in the specification include sequences encoding EPSPS and AHAS. See,

also, Figures 1-11, which provide representative chimeric oligonucleotides to target EPSPS and AHAS.

2. The amino acid sequence of both EPSPS and AHAS from various organisms were known in the art. See, for example, WO 96/33270 (provided as Appendix A in Amendment and Response filed June 21, 2004) and Friden *et al.* (provided as Appendix B in Amendment and Response filed June 21, 2004.) which provide amino acid sequences of AHAS from a variety of organisms including maize, tobacco, *Arabidopsis*, *Brassica, E. coli, S. typhimurium* and variants thereof. See, also, Padgette *et al.* (provided as Appendix C in Amendment and Response filed June 21, 2004) that confirms that EPSPS sequences from petunia, tomato, *Arabidopsis*, *Brassica napus*, soybean, maize, *E. coli, S. typhimurium*, *Aspergillus nidulans*, *Saccharomyces cerevisiae*, and *Bordetella pertussis* were characterized and sequenced.

3. Neuefeind *et al.* (1997) *Biol. Chem. 378*:199-205 (provided as Appendix D in Amendment and Response filed June 21, 2004) and Sherman *et al.* (1996) *Herbicide-Resistant Crops,* CRC Press Inc., 13-35 (provided as Appendix E in Amendment and Response filed June 21, 2004) clearly demonstrate various herbicide resistance genes were known in the art. Neuefeind *et al.* provide a review of plant Glutathione S-Transferases that confer resistance to a variety of herbicides including triazines, thiocarbamates, and chloroacetanilides (see, page 200, column 2). In addition, Neuefeind *et al.* provides a sequence alignment of nineteen (19) plant Glutathione S-Transferases and page 202, column 1 of Neuefeind *et al.* outlines the three subfamilies of Glutathione S-Transferases. Moreover, the herbicide triazine is further known to have an action on the ploastoquinone (PQ)-binding site of the D1 protein, encoded by the psbA gene. As illustrated on pages 22-23 of Sherman *et al.*, various sequences that confer resistance to triazine in the D1/D2 protein complex were known prior to the present invention. Sherman *et al.* further demonstrates that mitotic disruptor herbicides were known, as were target genes for these herbicides. For example, the gene encoding a modified tubulin of goosegrass was known. See page 18, paragraph 3 of Sherman *et al.* Phytoene desaturase inhibitors are also used as herbicides. As stated on page 27, paragraph 1 of Sherman *et al.*, the genes responsible for resistance to one of these herbicides were known prior to the present invention. It is therefore

clear that sequences that confer resistance to herbicides were known in the art prior to the filing date of the present invention.

In summary, based on the line of evidence presented above, it is clear that sequences that encode a polypeptide capable of conferring herbicide resistance were known to those of skill in the art as of the filing date of the present application, as were assays for determining if a sequence falls into this genus. Therefore, it is clear that the sequences targeted by the claimed methods are not new or unknown biological materials that ordinary skilled artisans would easily miscomprehend. The written description requirement under 35 U.S.C. §112, first paragraph, has been satisfied.

While the term "nucleotide sequence of interest encoding a polypeptide capable of conferring herbicide resistance in a plant," as is recited in claims 1 and 16, does not require a structure/function relationship between all member of the genus to satisfy the written description requirement as asserted by the Examiner, *Applicant emphasize that the claimed chimeric oligonucleotides encompassed by the genus do share a common structural and functional relationship.*

First, the chimeric oligonucleotide recited in claims 1 and 16 comprise a first block of RNA residues and a second block of RNA residues. The structure of the RNA segments present in the oligonucleotide simply depends on the nucleotide sequence of interest encoding a polypeptide capable of conferring herbicide resistance that is being targeted and the location of the desired alteration in the target sequence. As such, the RNA blocks recited in the claims do possess a common structure (*i.e.*, homology to the nucleotide sequence encoding a polypeptide capable of conferring herbicide resistance) and also a common function (*i.e.*, sufficient homology to allow the chimeric oligonucleotides to hybridize/bind to the target sequence).

Second, the chimeric oligonucleotide recited in claims 1 and 16 further recite that the chimeric oligonucleotide comprises "a block of DNA residues." The blocks of DNA residues also share a common structure (i.e., homology to a nucleotide sequence that encodes a polypeptide capable of conferring herbicide resistance in the plant and further

comprise a mismatch to the nucleotide sequence) and also a common function (i.e., the mismatch to the target sequence influences the repair machinery to alter the target sequence).

Third, the chimeric oligonucleotides recited in method claims 1 and 16 recite that the oligos are capable of forming a duplex structure; and, fourth, the chimeric oligonucleotides recited in method claims 1 and 16 each share a common function (i.e., they are capable of producing a nucleotide conversion in the nucleic acid molecule, whereby the nucleotide conversion in the nucleic acid molecule inactivates the nucleotide sequence of interest encoding the polypeptide capable of conferring herbicide resistance in the plant cell and thereby modulates the herbicide resistance of the plant or plant cell).

Applicants submit that a nucleotide sequence encoding a polypeptide "capable of conferring herbicide resistance" is a well-characterized term that would not be miscomprehended by one of skill in the art. Moreover, the chimeric oligonucleotides recited in the claimed methods share a common structural and functional relationship. Accordingly, sufficient description has been provided to demonstrate possession of the claimed invention. In view of the evidence provided above, claims 1-3, 6-7, 9-10, 13-20, 23-24, and 27-29 satisfy the requirements of 35 U.S.C. §112, first paragraph, and the rejection should be withdrawn.

II. Claims 9 and 23 are drawn to a method that employs a chimeric oligonucleotide comprising a first and a second block of RNA residues that are homologous to the nucleotide sequence of interest, wherein the nucleotide sequence of interest "is a 5-enol pyruvylshikimate-3-phosphate synthase (EPSPS) gene." To expedite prosecution, independent claims 1 and 16 have been amended to recite that the chimeric oligonucleotide when introduced into the plant or plant cells is capable of producing a nucleotide conversion in said nucleic acid molecule that "inactivates the nucleotide sequence of interest encoding the polypeptide capable of conferring herbicide resistance in the plant cell and thereby modulates the herbicide resistance" of the plant or plant cell.

First, every species encompassed by the claimed invention need not be disclosed in the specification to satisfy the written description requirement of 35 U.S.C. § 112, first paragraph. *Utter v. Hiraga*, 845 F.2d 993, 6 USPQ2d 1709 (Fed. Cir. 1988). In fact, the Examiner is reminded that information that is well known in the art need not be described in detail in the specification. As evidence that many EPSPS sequences were known and characterized in the art from a variety of diverse species at the time of filing, Applicants provide Padgette *et al.* (provided as Appendix C in Amendment and Response filed June 21, 2004). Padgette demonstrates that EPSPS sequences from petunia, tomato, *Arabidopsis*, *Brassica napus*, soybean, maize, *E. coli, S. typhimurium*, *Aspergillus nidulans*, *Saccharomyces cerevisiae*, and *Bordetella pertussis* were characterized and sequenced. Therefore, EPSPS polypeptides from higher plants, bacteria, and fungi were known in the art prior to the present invention.

Second, one skilled in the art is clearly apprised of desirable alterations that are capable of inactivating the sequence of interest and thereby modulating resistance to EPSPS. For example, in view of the disclosure provided in the specification, chimeric oligonucleotides could be designed to contain a block of DNA residues that introduce a stop mutation or a frame shift mutation into the EPSPS sequence. Alternatively, the block of DNA residues could be designed to allow for the alteration of regulatory regions that influence expression of the EPSPS sequence. Moreover, additional alterations (i.e., dominant and recessive mutations) could be made to inactive the sequence. In view of the disclosure in the specification and the general level of knowledge in the art, one of skill in the art would be well apprised of mutations that are capable of inactivating the nucleotide sequence of interest (i.e., affecting the activity and/or the expression of the sequence in a desired manner) and therefore capable of designing chimeric oligonucleotides comprising an appropriate block of DNA residues that would alter the target sequence accordingly.

The Federal Circuit has made it clear that sufficient written description requires simply the knowledge and level of skill in the art to permit one of skill to immediately envision the product claimed from the disclosure. *Purdue Pharm L.P. v. Faulding In.*, 230 F.3d 1320 1323, 596 USPQ2d 1481, 1483 (Fed. Cir. 2000) ("One skilled in the art must immediately discern the

limitations at issue in the claims."). As demonstrated above, the art was aware of both the structural and functional characteristics of the EPSPS enzyme class to distinguish the claimed invention from other materials, as well as assays to assay for the inactivation of the sequence. One of skill in the art would conclude that the applicant was in possession of the claimed species. The requirement under 35 U.S.C. §112, first paragraph, for claims 9 and 23 have been satisfied.

III. Claims 10 and 24 are drawn to a chimeric oligonucleotide comprising a first and a second block of RNA residues that are homologous to a nucleotide sequence that is capable of conferring herbicide resistance in a plant, wherein nucleotide sequence is AHAS.

The instant specification successfully designed chimeric oligonucleotides that conferred resistance in plants to both imidazolinone and sulfonylurea by altering amino the amino acid sequence of AHAS. See, Table 2. Again, the Examiner is reminded that information that is well known in the art need not be described in detail in the specification. As evidence that sequences capable of conferring resistance to imidazolinone and sulfonylurea were known in the art Applicants provide WO 96/33270 (provided as Appendix A in Amendment and Response filed June 21, 2004) that is drawn to structure based modeling methods for the preparation of AHAS variants. Figure 5 of the WO 96/33270 publication provides an alignment of AHAS polypeptides from a variety of plants including maize, tobacco, *Arabidopsis*, and *Brassica*. In addition, AHAS sequences from *E. coli* and *S. typhimurium* were also characterized at the time of filing. See, Friden *et al.*, Figure 5 (provided as Appendix B in Amendment and Response filed June 21, 2004). Therefore, AHAS polypeptides from higher plants, bacteria, and fungi have been characterized and sequenced.

In addition, independent claims 1 and 16 have been amended to recite that the nucleotide conversion in the nucleic acid molecule "modulates the herbicide resistance of said plant." As outlined above, alterations that are capable of modulating herbicide resistance by inactivating AHAS were known in the art. As amended, the genus encompassed by claims 10 and 24 satisfy the written description requirements of 35 U.S.C. §112, first paragraph, and the rejection should be withdrawn.

Enablement

Claims 1-26 were rejected under 35 U.S.C. §112, first paragraph, for lack of enablement. This rejection is respectfully traversed.

I. Claims 11, 12, 25, and 26 were rejected for lack of enablement for being drawn to methods that employ oligonucleotides that do not "inactivate" the nucleotide sequence of interest. Claims 11, 12, 25, and 26 have been canceled.

II. In support of the rejection of claims 1-26 for lack of enablement, the Examiner states that the data in the specification demonstrates the successful targeting of AHAS165 and PAT/GFP were "due to substitutions of different nucleotides [than those altered in the chimeric oligonucleotide], and thus were not predicted" (page 8, lines 1-3, Office Action, mailed March 19, 2004).

Claims 1 and 16 do not recite that that the conversion is "predicted." Instead, the claims of the present invention recite that the chimeric oligonucleotide recognizes and implements a nucleotide conversion in the nucleic acid molecule, "whereby the nucleotide conversion in said nucleic acid molecule inactivates the nucleotide sequence of interest encoding the polypeptide capable of conferring herbicide resistance in the plant cell [or plant] and thereby modulates the herbicide resistance" of the plant or plant cell. One of skill in the art could readily select for the described phenotype (i.e., a modulated resistance to a herbicide) and practice the claimed invention. Methods for this type of phenotypic selection were known in the art, and in fact, Applicants provide representative selection schemes for modulating herbicide resistance for glyphosate, imidazolinone, and sulfonylurea in the instant specification. Accordingly, contrary to the assertions in the Office Action, the claims are enabled to implement a nucleotide conversion, "whereby the nucleotide conversion in the nucleic acid molecule modulates herbicide resistance."

Claims 6, 7, 19 and 20 recite that the chimeric oligonucleotide introduces a frameshift or a premature stop codon. The Examiner is reminded that the Federal Circuit has repeatedly stated that enablement is not precluded by the necessity for some experimentation, so long as the experimentation needed to practice the invention is not undue. *In re Wands,* 8 USPQ2d 1400 (Fed Cir 1988). Furthermore, a considerable amount of experimentation is permissible, if it is merely routine, or if the specification provides a reasonable amount of guidance in which the experimentation should proceed. *Id.* As the target sequence is known and the screening methods are adequately described in the specification and known in the art, identification of these specific classes of mutations is nothing more than routine experimentation analogous to the hybridoma screening the Federal Circuit found acceptable in *In re Wands* (858 F.2d 731,8 USPQ 1400(Fed. Cir. 1988)).

III. The Examiner further asserts the claimed methods of the present invention require undue experimentation. The Examiner's cites three lines of evidence to support this conclusion.

a. The Examiner cites Beetham *et al.* to support the conclusion of undue experimentation. Beetham *et al.* found that the modified base in the Pro-196 codon was always found to be one nucleotide 5' of the mismatch (page 8776, right column, 3rd paragraph). The Examiner further cites Kochevenko *et al.* which found that depending on the target site, multiple codon changes could occur that were not predicted (see, Table 1, page 179). See, page 9, lines 1-3 of Office Action mailed March 19, 2004.

First, claims 1 and 16 do *not* recite that the mismatch in the DNA block is introduced into the target sequence. The claims state only that the block of DNA residues comprise at least one mismatch to the nucleic acid molecule (i.e., the target sequence). In fact, this point is clarified on page 9, lines 27-21 which states:

> Furthermore, the methods can be used to create a predetermined nucleotide pair mismatch in a target sequence of the genome of a plant or plant cell upon which endogenous mismatch repair mechanisms can operate to create a nucleotide alteration at or near the target sequence.

So while the mismatch appearing in the DNA block is predetermined, the alteration in the target sequence simply requires a selectable change in the modulation of the herbicide resistance of the plant or plant cell. Both Beetham *et al.* and Kochevenko *et al.* succeed in creating a nucleotide alteration at or near the target sequence, as does the data appearing in the present application. See, table 2, page 26. All evidence of record clearly establishes that the claimed methods do not require undue experimentation.

To expedite prosecution, independent claims 1 and 16 have been amended to recite that the chimeric oligonucleotide is capable of recognizing and implementing a nucleotide conversion in the nucleic acid molecule, "whereby said nucleotide conversion in said nucleic acid molecule inactivates the nucleotide sequence of interest encoding the polypeptide capable of conferring herbicide resistance in the plant cell [or plant] and thereby modulates the herbicide resistance" of the plant or plant cells. *Again, it is pointed out that Beetham et al., Kochevenko et al., and the present application demonstrate the successful modulation of herbicide resistance in a plant.* The art cited by the Examiner therefore does not render the experimentation needed to practice the methods undue, and instead, the cited art provides direct evidence of the success of the technique.

b. The Examiner further cites Hohn *et al.* (1999) *Proc. Natl. Acad. Sci. 96*:8321-8323 in support of the conclusion that the methods require undue experimentation. Hohn *et al.* teach that unexpected changes in gene sequence occurred using the chimeric oligonucleotide. Applicants draw the Examiner's attention to page 8322, column 1 of the reference, in which Hohn *et al.* states that the efficiencies of recovery of chlorsulfuron-resistant tobacco clones was 10 to 20 times above background and about 4 and 15 times above background for imazethapyr- and chlorsulfuron-resistant maize clones, respectively. Hohn *et al.* further states that these "*frequencies are acceptable for selectable targeted mutations in plants*" (emphasis added, page 8322, column 1, last three lines of first paragraph). In addition, Hohn *et al.* further summarizes the results from various studies using chimeric oligonucleotides in plants. In all instances, alterations at or near the mismatch in the target gene were generated (page 8322, column 1,

paragraph 2 and column 2), and moreover, *plants having a modulated herbicide resistance were isolated in all scenarios.* As such, Hohn *et al.* does not support the assertion that the methods of claims 1-26 would require undue experimentation.

c. The Examiner further states that the art teaches that the efficiency of the gene correction process using chimeric oligonucleotides may be influenced by the differential regulation of mismatches by repair enzymes and possible sequence context effects (Anderson *et al.* (2002) *J. Mol. Med. 80*:770-781, page 770, right column). These conclusions were drawn due to the fact that the chimeric oligonucleotides can produce different types of alterations other than the predetermined mismatch appearing in the chimeric oligonucleotide. For the identical reasons addressed above with Hohn *et al.*, these statements by Anderson *et al.* are not sufficient to conclude that the claimed methods require undue experimentation.

The Examiner further states that Anderson *et al.* teaches that the correction efficiencies of mutated bases are in most cases still inadequate for clinical use, and a considerable variation (0.003-60%) in the degree of correction has been reported both *in vitro* and *in vivo*. These statements by Anderson *et al.* are not relevant to the issue of undue experimentation. First, the claimed chimeric oligonucleotides of the present invention are not for "clinical use" in humans, in which the degree of correction would play an important role in the success of the technique. The claims of the present invention recite that the chimeric oligonucleotide is used in a plant or plant cell. Again, even Hohn *et al.* concluded that "*the frequencies are acceptable for selectable targeted mutations in plants*" (emphasis added, page 8322, column 1, last three lines of first paragraph).

While ample disclosure provided in the specification along with the success of this technique was made of record in the Response to Office Action mailed 7/28/03, Applicants reproduce the table below simply to reemphasize that the claimed method of using the chimeric oligonucleotides is successful in plants.

Table 1.

Reference	Target Site Modified	Pages of Reference
Beetham *et al.*	Pro196 of ALS gene	p. 8777, column 2, paragraph 2
Beetham *et al.*	Codon 6 of GFP transgene integrated into genome	p. 8778, column 1; p8875, column 1, lines 4-5
Kochevonko *et al*	Try573 of ALS gene	Table 1, p. 179
Kochevonko *et al*	Pro196 of ALS gene	Table 1, p. 179
Present application	Ser621 of AHAS	Table 2, page 26
Present application	Pro165 of AHAS	Table 2, page 26
Present application	**nt 2987-2990 (end of coding region) of GFP transgene integrated into genome.	Table 2, page 26; page 28, lines 2-3; page 27, lines 25-35
Present application	**nt 2987-2990 (end of coding region) of GFP transgene integrated into genome.	Table 2, page 26 page 28, lines 2-3; page 27, lines 25-35

** Experiment performed on two independent GFP transgenic lines. Thus, modification of the GFP constructs represents successful targeting at two independent genomic locations.

The data summarized in Table 1 provides evidence for the successful targeting of 7 *independent genomic positions in both monocots and dicots*, Applicants have provided clear evidence that, contrary to the assertions by the Examiner, the disclosure in the specification is correlative of the ability to use the chimeric oligonucleotide of the present invention to target a variety of genes including, genes that are capable of conferring herbicide resistance.

In summary, in view of the amendments made to the claims, the disclosure in the instant specification is correlative of the ability to use the chimeric oligonucleotides of the present invention to modify a target gene that is capable of conferring resistance to herbicides. The Examiner is reminded that the Federal Circuit has repeatedly stated that enablement is not precluded by the necessity for some experimentation, so long as the experimentation needed to practice the invention is not undue. *In re Wands,* 8 USPQ2d 1400 (Fed Cir 1988). Furthermore, a considerable amount of experimentation is permissible, if it is merely routine, or if the specification provides a reasonable amount of guidance in which the experimentation should proceed. *Id. See also Johns Hopkins University v. Cellpro*, 931 F. Supp. 303, 324 (D. Del.

1996), *aff'd in part, vacated in part, & remanded*, 47 U.S.P.Q.2d 1705 (Fed. Cir. 1998) ("The specification need only enable one mode of making the claimed invention."). The methods recited in claims 1-26 satisfy the requirements of 35 U.S.C. §112, first paragraph, and the rejection for lack of enablement should be withdrawn.

The Rejection of the Claims Under 35 U.S.C. §103 Should Be Withdrawn

Claims 1-10, 13-24, and 27-29 were rejected under 35 U.S.C. §103(a) as being unpatentable over U.S. Patent No. 5,731,181 in view of Dale *et al.* (1991) *Proc. Natl. Acad. Sci. 88*:10558-10562. This rejection is respectfully traversed.

U.S. Patent No. 5,731,181 is drawn to chimeric oligonucleotides and methods of use. U.S. Patent No. 5,731,181 suggests the use the oligonucleotides in plants, but offers no suggestion to target sequences that encode polypeptides capable of conferring herbicide resistance in a plant.

Dale *et al.* teaches the use of a Cre/Lox system to remove a hygromycin phosphotransferase (hpt) selectable marker from a tobacco plant.

The cited references do not provide motivation to one of ordinary skill in the art to make the modification or combination and arrive at the methods of the claimed invention. Dale *et al.* teaches the successful removal of the hpt selectable marker from a tobacco plant using the Cre/Lox recombination system. However, no relationship was suggested in the prior art between inactivating a nucleotide sequence encoding a polypeptide capable of conferring herbicide resistance in a plant and employing chimeric oligonucleotides to alter such sequences. In fact, Dale *et al.* provides a successful method for removing sequences of interest using the Cre/Lox system. There would have been no reason for one of ordinary skill in the art to modify the teachings of Dale *et al.* and use chimeric oligonucleotides, as taught by U.S. Patent No. 5,731,181. Accordingly, while Dale *et al.* teach generally the removal of selectable markers using a recombination system, there was no teaching or motivation that one should use a chimeric oligonucleotide to inactivate a selectable marker. The prior art cited by the Examiner

therefore does not provide any impetus to carry out the methods set forth in claims 1-29 of the instant application. The Examiner is respectfully requested to withdraw the rejection.

It is further noted that claims 9, 10, 23, and 24 are drawn to the inactivation of EPSPS and AHAS. Neither U.S. Patent No. 5,731,181 nor Dale *et al.* provide any guidance to one of skill in the art to inactive the nucleotide sequences recited in these method claims. Accordingly, claims 9, 10, 23, and 24 are not obvious in view of the cited art and the Examiner is respectfully requested to withdraw the rejection.

Applicants further note the contradiction of the §112 first paragraph rejections (written description and enablement) with the obviousness rejection, both of which appear in the March 19, 2004 Office Action. On one hand, the Examiner argues that the methods of using the chimeric oligonucleotides are not sufficiently described or enabled, while on the other hand, the Examiner asserts that the use of the methods to target sequences capable of conferring herbicide resistance was obvious. If the method is considered obvious, how can the method not be sufficiently described or enabled, or vice versa? Applicants were obligated to file a complete response and therefore addressed each rejection. While Applicant earnestly believes all rejections should be withdrawn, if the rejections are not withdrawn, the Examiner is respectfully requested to review the obviousness rejection and the §112 1st paragraph rejection and proceed with only one rejection.

CONCLUSIONS

The Examiner is respectfully requested to withdraw the rejections and allow claims 1-3, 6-7, 9-10, 13-20, 23-24 and 27-29. Early notice to this effect is solicited.

It is not believed that extensions of time or fees for net addition of claims are required, beyond those that may otherwise be provided for in documents accompanying this paper. However, in the event that additional extensions of time are necessary to allow consideration of this paper, such extensions are hereby petitioned under 37 CFR § 1.136(a), and any fee required therefore (including fees for net addition of claims) is hereby authorized to be charged to Deposit Account No. 16-0605.

Respectfully submitted,

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CERTIFICATE OF FACSIMILE TRANSMISSION

I hereby certify that this paper is being facsimile transmitted to the US Patent and Trademark Office, at FAX No. 703-872-9306 on October 22, 2004.

Pamela Lockley

RTA01/2167271v1

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NOTICE OF ALLOWANCE AND FEE(S) DUE

29122 7590 01/12/2005

ALSTON & BIRD LLP
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101 SOUTH TYRON STREET, SUITE 4000
CHARLOTTE, NC 28280-4000

EXAMINER	
KRUSE, DAVID H	
ART UNIT	PAPER NUMBER
1638	

DATE MAILED: 01/12/2005

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/579,784	05/26/2000	Christopher L. Baszczynski	5718-23B	9894

TITLE OF INVENTION: TARGETED MANIPULATION OF GENES IN PLANTS

APPLN. TYPE	SMALL ENTITY	ISSUE FEE	PUBLICATION FEE	TOTAL FEE(S) DUE	DATE DUE
nonprovisional	NO	$1400	$0	$1400	04/12/2005

THE APPLICATION IDENTIFIED ABOVE HAS BEEN EXAMINED AND IS ALLOWED FOR ISSUANCE AS A PATENT. PROSECUTION ON THE MERITS IS CLOSED. THIS NOTICE OF ALLOWANCE IS NOT A GRANT OF PATENT RIGHTS. THIS APPLICATION IS SUBJECT TO WITHDRAWAL FROM ISSUE AT THE INITIATIVE OF THE OFFICE OR UPON PETITION BY THE APPLICANT. SEE 37 CFR 1.313 AND MPEP 1308.

THE ISSUE FEE AND PUBLICATION FEE (IF REQUIRED) MUST BE PAID WITHIN THREE MONTHS FROM THE MAILING DATE OF THIS NOTICE OR THIS APPLICATION SHALL BE REGARDED AS ABANDONED. THIS STATUTORY PERIOD CANNOT BE EXTENDED. SEE 35 U.S.C. 151. THE ISSUE FEE DUE INDICATED ABOVE REFLECTS A CREDIT FOR ANY PREVIOUSLY PAID ISSUE FEE APPLIED IN THIS APPLICATION. THE PTOL-85B (OR AN EQUIVALENT) MUST BE RETURNED WITHIN THIS PERIOD EVEN IF NO FEE IS DUE OR THE APPLICATION WILL BE REGARDED AS ABANDONED.

HOW TO REPLY TO THIS NOTICE:

I. Review the SMALL ENTITY status shown above.

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If the SMALL ENTITY is shown as NO:

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B. If applicant claimed SMALL ENTITY status before, or is now claiming SMALL ENTITY status, check box 5a on Part B - Fee(s) Transmittal and pay the PUBLICATION FEE (if required) and 1/2 the ISSUE FEE shown above.

II. PART B - FEE(S) TRANSMITTAL should be completed and returned to the United States Patent and Trademark Office (USPTO) with your ISSUE FEE and PUBLICATION FEE (if required). Even if the fee(s) have already been paid, Part B - Fee(s) Transmittal should be completed and returned. If you are charging the fee(s) to your deposit account, section "4b" of Part B - Fee(s) Transmittal should be completed and an extra copy of the form should be submitted.

III. All communications regarding this application must give the application number. Please direct all communications prior to issuance to Mail Stop ISSUE FEE unless advised to the contrary.

IMPORTANT REMINDER: Utility patents issuing on applications filed on or after Dec. 12, 1980 may require payment of maintenance fees. It is patentee's responsibility to ensure timely payment of maintenance fees when due.

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Complete and send this form, together with applicable fee(s), to: Mail **Mail Stop ISSUE FEE**
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29122 7590 01/12/2005

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(Depositor's name)

(Signature)

(Date)

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/579,784	05/26/2000	Christopher L. Baszczynski	5718-23B	9894

TITLE OF INVENTION: TARGETED MANIPULATION OF GENES IN PLANTS

APPLN. TYPE	SMALL ENTITY	ISSUE FEE	PUBLICATION FEE	TOTAL FEE(S) DUE	DATE DUE
nonprovisional	NO	$1400	$0	$1400	04/12/2005

EXAMINER	ART UNIT	CLASS-SUBCLASS
KRUSE, DAVID H	1638	800-278000

1. Change of correspondence address or indication of "Fee Address" (37 CFR 1.363).

☐ Change of correspondence address (or Change of Correspondence Address form PTO/SB/122) attached.

☐ "Fee Address" indication (or "Fee Address" Indication form PTO/SB/47; Rev 03-02 or more recent) attached. **Use of a Customer Number is required.**

2. For printing on the patent front page, list

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3. ASSIGNEE NAME AND RESIDENCE DATA TO BE PRINTED ON THE PATENT (print or type)

PLEASE NOTE: Unless an assignee is identified below, no assignee data will appear on the patent. If an assignee is identified below, the document has been filed for recordation as set forth in 37 CFR 3.11. Completion of this form is NOT a substitute for filing an assignment.

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Please check the appropriate assignee category or categories (will not be printed on the patent) : ☐ Individual ☐ Corporation or other private group entity ☐ Government

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5. **Change in Entity Status** (from status indicated above)

☐ a. Applicant claims SMALL ENTITY status. See 37 CFR 1.27.

☐ b. Applicant is no longer claiming SMALL ENTITY status. See 37 CFR 1.27(g)(2).

The Director of the USPTO is requested to apply the Issue Fee and Publication Fee (if any) or to re-apply any previously paid issue fee to the application identified above.
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This collection of information is required by 37 CFR 1.311. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 12 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, Virginia 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450.

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29122 7590 01/12/2005

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EXAMINER	
KRUSE, DAVID H	

ART UNIT	PAPER NUMBER
1638	

DATE MAILED: 01/12/2005

Determination of Patent Term Extension under 35 U.S.C. 154 (b)
(application filed after June 7, 1995 but prior to May 29, 2000)

The Patent Term Extension is 0 day(s). Any patent to issue from the above-identified application will include an indication of the 0 day extension on the front page.

If a Continued Prosecution Application (CPA) was filed in the above-identified application, the filing date that determines Patent Term Extension is the filing date of the most recent CPA.

Applicant will be able to obtain more detailed information by accessing the Patent Application Information Retrieval (PAIR) WEB site (http://pair.uspto.gov).

Any questions regarding the Patent Term Extension or Adjustment determination should be directed to the Office of Patent Legal Administration at (571) 272-7702. Questions relating to issue and publication fee payments should be directed to the Customer Service Center of the Office of Patent Publication at (703) 305-8283.

PTOL-85 (Rev. 12/04) Approved for use through 04/30/2007.

Notice of Allowability

Application No.	Applicant(s)	
09/579,784	BASZCZYNSKI ET AL.	
Examiner	**Art Unit**	
David H Kruse	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to *the Amendment filed 22 October 2004*.

2. ☒ The allowed claim(s) is/are *1-3,6,7,9,10,13-20,23,24 and 27-29*.

3. ☒ The drawings filed on *26 May 2000* are accepted by the Examiner.

4. ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
   a) ☐ All b) ☐ Some* c) ☐ None of the:
   1. ☐ Certified copies of the priority documents have been received.
   2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
   3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

   * Certified copies not received: _____.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.
THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

5. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.

6. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
   (a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached
   1) ☐ hereto or 2) ☐ to Paper No./Mail Date _____.
   (b) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date _____.

   Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).

7. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

1. ☐ Notice of References Cited (PTO-892)
2. ☐ Notice of Draftperson's Patent Drawing Review (PTO-948)
3. ☐ Information Disclosure Statements (PTO-1449 or PTO/SB/08), Paper No./Mail Date _____
4. ☐ Examiner's Comment Regarding Requirement for Deposit of Biological Material
5. ☐ Notice of Informal Patent Application (PTO-152)
6. ☐ Interview Summary (PTO-413), Paper No./Mail Date _____ .
7. ☐ Examiner's Amendment/Comment
8. ☐ Examiner's Statement of Reasons for Allowance
9. ☐ Other _____.

DAVID H. KRUSE, PH.D.
PATENT EXAMINER

PTO/SB/44 (04-05)
Approved for use through 04/30/2007. OMB 0651-0033
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

(Also Form PTO-1050)

UNITED STATES PATENT AND TRADEMARK OFFICE

CERTIFICATE OF CORRECTION

PATENT NO. : 6,911,575 B1

APPLICATION NO.: 09/579,784

ISSUE DATE : June 28, 2005

INVENTOR(S) : Christopher L. Baszczynski et al.

It is certified that error appears in the above-identified patent and that said Letters Patent are hereby corrected as shown below:

Column 33
Lines 13-47, should read as follows:
--3. A method to inactivate a nucleotide sequence of interest introduced into a genome of a plant cell, said method comprising:

transforming said plant cell with a nucleic acid molecule comprising a promoter operably linked to said nucleotide sequence of interest encoding a polypeptide capable of conferring herbicide resistance in the plant cell; and

introducing into said plant cell at least one chimeric oligonucleotide, said chimeric oligonucleotide having at least a first block of RNA residues, and a second block of RNA residues, wherein said first and said second block of RNA residues are homologous to said nucleic acid molecule; said first and said second block of RNA residues are each about 3 nucleotides to about 20 nucleotides in length and are contiguous with and flank a block of DNA residues, wherein the block of DNA residues comprises at least one mismatch to the nucleic acid molecule and said block of DNA residues is about 5 nucleotides to about 60 nucleotides in length; wherein said first RNA block, said DNA block and said second RNA block are identical to a contiguous sequence of the nucleic acid molecule except for the presence of said mismatch in said DNA block; said chimeric oligonucleotide comprises additional DNA residues that are capable of forming a duplex structure with said first block of RNA residues, said block of DNA residues, and said second block of RNA residues; and, said chimeric oligonucleotide being capable of recognizing and implementing a nucleotide conversion in said nucleic acid molecule, whereby said nucleotide conversion in said nucleic acid molecule inactivates the nucleotide sequence of interest encoding the polypeptide capable of conferring herbicide resistance in the plant cell and thereby modulates the herbicide resistance of said plant cell.--

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CERTIFICATE OF CORRECTION

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